

Amendments to the Specification

Please replace paragraph [0087] with the following paragraph:

EXAMPLE 1

Volatilization of Alprazolam

[0087] A solution of 2.6 mg alprazolam in 120 μ L dichloromethane was coated on a 3.6 cm x 8 cm piece of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the alprazolam coating on the 28.8 cm² aluminum solid support, after solvent evaporation, is about 0.9 microns. The coated foil was wrapped around a 300 watt halogen tube (Feit Electric Company, Pico Rivera, CA), which was inserted into a glass tube sealed at one end with a rubber stopper. Running 75 V of alternating current (driven by line power controlled by a variac) through the bulb for 6 s afforded alprazolam thermal vapor (including alprazolam aerosol), which collected on the glass tube walls. Reverse-phase HPLC analysis with detection by absorption of 225 nm light showed the collected material to be at least 99.9% pure alprazolam. To obtain higher purity aerosols, one can coat a lesser amount of drug, yielding a thinner film to heat. A linear decrease in film thickness is associated with a linear decrease in impurities.

Please replace paragraph [0088] with the following paragraph:

EXAMPLE 2

Volatilization of Estazolam

[0088] A solution of 2.0 mg estazolam in 120 μ L dichloromethane was coated on a 3.6 cm x 8 cm piece of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the estazolam coating on the 28.8 cm² aluminum solid support, after solvent evaporation, is about 0.7 microns. The coated foil was wrapped around a 300 watt halogen tube (Feit Electric Company, Pico Rivera, CA), which was inserted into a glass tube sealed at one end with a rubber stopper. Running 60 V of alternating current (driven by line power controlled by a variac) through the bulb for 3 s, followed by 45 V for 11s, afforded estazolam thermal vapor (including estazolam aerosol), which collected on the glass tube walls. Reverse-phase HPLC analysis with detection by absorption of 225 nm light showed the collected material to be at least 99.9% pure estazolam.

Please replace paragraph [0089] with the following paragraph:

EXAMPLE 3

Volatilization of Midazolam

[0089] A solution of 5.0 mg midazolam in 120 μ L dichloromethane was coated on a 3.6 cm x 8 cm piece of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the midazolam coating on the 28.8 cm² aluminum solid support, after solvent evaporation, is about 1.7 microns. The coated foil was wrapped around a 300 watt halogen tube (Feit Electric Company, Pico Rivera, CA), which was inserted into a glass tube sealed at one end with a rubber stopper. Running 60V of alternating current (driven by line power controlled by a variac) through the bulb for 6 s afforded midazolam thermal vapor (including midazolam aerosol), which collected on the glass tube walls. Reverse-phase HPLC analysis with detection by absorption of 225 nm light showed the collected material to be at least 99.9% pure midazolam.

Please replace paragraph [0090] with the following paragraph:

EXAMPLE 4

Particle Size, Particle Density, and Rate of Inhalable Particle Formation of Midazolam Aerosol

[0090] A solution of 17.1 mg midazolam in 200 μ L dichloromethane was spread out in a thin layer on the central portion of a 4 cm x 9 cm sheet of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the midazolam coating on the 36 cm² aluminum solid support, after solvent evaporation, is about 4.8 microns. The aluminum foil was wrapped around a 300 watt halogen tube, which was inserted into a T-shaped glass tube. One of the openings of the tube was sealed with a rubber stopper, another was loosely covered with the end of the halogen tube, and the third was connected to a 1 liter, 3-neck glass flask. The glass flask was further connected to a large piston capable of drawing 1.1 liters of air through the flask. Alternating current was run through the halogen bulb by application of 90 V using a variac connected to 110 V line power. Within 1 s, an aerosol appeared and was drawn into the 1 L flask by use of the piston, with collection of the aerosol terminated after 6 s. The aerosol was analyzed by connecting the 1 L flask to an eight-stage Andersen non-viable cascade impactor. Results are shown in table 1. MMAD of the collected aerosol was 2.8 microns with a geometric standard deviation of 1.9. Also shown in table 1 is the number of

particles collected on the various stages of the cascade impactor, given by the mass collected on the stage divided by the mass of a typical particle trapped on that stage. The mass of a single particle of diameter D is given by the volume of the particle, $\pi D^3/6$, multiplied by the density of the drug (taken to be 1 g/cm^3). The inhalable aerosol particle density is the sum of the numbers of particles collected on impactor stages 3 to 8 divided by the collection volume of 1 L, giving an inhalable aerosol particle density of 5.5×10^7 particles/mL. The rate of inhalable aerosol particle formation is the sum of the numbers of particles collected on impactor stages 3 through 8 divided by the formation time of 6 s, giving a rate of inhalable aerosol particle formation of 9.1×10^9 particles/second.

Please replace paragraph [0092] with the following paragraph:

EXAMPLE 5

Drug Mass Density and Rate of Drug Aerosol Formation of Midazolam Aerosol

[0092] A solution of 16.7mg midazolam in 200 μL dichloromethane was spread out in a thin layer on the central portion of a 4 cm x 9 cm sheet of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the midazolam coating on the 36 cm² aluminum solid support, after solvent evaporation, is about 4.6 microns. The aluminum foil was wrapped around a 300 watt halogen tube, which was inserted into a T-shaped glass tube. One of the openings of the tube was sealed with a rubber stopper, another was loosely covered with the end of the halogen tube, and the third was connected to a 1 liter, 3-neck glass flask. The glass flask was further connected to a large piston capable of drawing 1.1 liters of air through the flask. Alternating current was run through the halogen bulb by application of 90 V using a variac connected to 110 V line power. Within seconds, an aerosol appeared and was drawn into the 1 L flask by use of the piston, with formation of the aerosol terminated after 6 s. The aerosol was allowed to sediment onto the walls of the 1 L flask for approximately 30 minutes. The flask was then extracted with dichloromethane and the extract analyzed by HPLC with detection by light absorption at 225 nm. Comparison with standards containing known amounts of midazolam revealed that 8.12 mg of > 99% pure midazolam had been collected in the flask, resulting in an aerosol drug mass density of 8.12 mg/L. The aluminum foil upon which the midazolam had previously been coated was weighed following the experiment. Of the 16.7 mg originally coated on the aluminum, all of the material was found to have aerosolized in the 6 s time period, implying a rate of drug aerosol formation of 2.7 mg/s.

Please replace paragraph [0093] with the following paragraph:

EXAMPLE 6

Volatilization of Triazolam

[0093] A solution of 2.0 mg triazolam in 120 μ L dichloromethane was coated on a 3.6 cm x 8 cm piece of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the triazolam coating on the 28.8 cm² aluminum solid support, after solvent evaporation, is about 0.7 microns. The coated foil was wrapped around a 300 watt halogen tube (Feit Electric Company, Pico Rivera, CA), which was inserted into a glass tube sealed at one end with a rubber stopper. Running 75 V of alternating current (driven by line power controlled by a variac) through the bulb for 2 s, followed by 45 V for 8 s, afforded triazolam thermal vapor (including triazolam aerosol), which collected on the glass tube walls. Reverse-phase HPLC analysis with detection by absorption of 225 nm light showed the collected material to be at least 99.85% pure triazolam.

Please replace paragraph [0094] with the following paragraph:

EXAMPLE 7

Particle Size, Particle Density, and Rate of Inhalable Particle Formation of Triazolam Aerosol

[0094] A solution of 16.4 mg triazolam in 200 μ L dichloromethane was spread out in a thin layer on the central portion of a 4 cm x 9 cm sheet of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the triazolam coating on the 36 cm² aluminum solid support, after solvent evaporation, is about 4.6 microns. The aluminum foil was wrapped around a 300 watt halogen tube, which was inserted into a T-shaped glass tube. One of the openings of the tube was sealed with a rubber stopper, another was loosely covered with the end of the halogen tube, and the third was connected to a 1 liter, 3-neck glass flask. The glass flask was further connected to a large piston capable of drawing 1.1 liters of air through the flask. Alternating current was run through the halogen bulb by application of 90 V using a variac connected to 110 V line power. Within 1 s, an aerosol appeared and was drawn into the 1 L flask by use of the piston, with collection of the aerosol terminated after 6 s. The aerosol was analyzed by connecting the 1 L flask to an eight-stage Andersen non-viable cascade impactor. Results are shown in table 1. MMAD of the collected aerosol was 2.2 microns with a geometric standard deviation of 2. Also shown in table 1 is the number of particles collected on the various stages of the cascade impactor, given by the mass collected on the stage

divided by the mass of a typical particle trapped on that stage. The mass of a single particle of diameter D is given by the volume of the particle, $\pi D^3/6$, multiplied by the density of the drug (taken to be 1 g/cm^3). The inhalable aerosol particle density is the sum of the numbers of particles collected on impactor stages 3 to 8 divided by the collection volume of 1 L, giving an inhalable aerosol particle density of 3.8×10^6 particles/mL. The rate of inhalable aerosol particle formation is the sum of the numbers of particles collected on impactor stages 3 through 8 divided by the formation time of 6 s, giving a rate of inhalable aerosol particle formation of 6×10^8 particles/second.

Please replace paragraph [0096] with the following paragraph:

EXAMPLE 8

Drug Mass Density and Rate of Drug Aerosol Formation of Triazolam Aerosol

[0096] A solution of 0.6 mg triazolam in 200 μL dichloromethane was spread out in a thin layer on the central portion of a 4 cm x 9 cm sheet of aluminum foil. The dichloromethane was allowed to evaporate. Assuming a drug density of about 1g/cc, the calculated thickness of the triazolam coating on the 36 cm² aluminum solid support, after solvent evaporation, is about 0.2 microns. The aluminum foil was wrapped around a 300 watt halogen tube, which was inserted into a T-shaped glass tube. One of the openings of the tube was sealed with a rubber stopper, another was loosely covered with the end of the halogen tube, and the third was connected to a 1 liter, 3-neck glass flask. The glass flask was further connected to a large piston capable of drawing 1.1 liters of air through the flask. Glass wool was placed in the tube connecting the flask to the piston. Alternating current was run through the halogen bulb by application of 90 V using a variac connected to 110 V line power. Within seconds, an aerosol appeared and was drawn into the 1 L flask by use of the piston, with formation of the aerosol terminated after 6 s. The aerosol was allowed to sediment onto the walls of the 1 L flask for approximately 30 minutes. The flask and glass wool were then extracted with dichloromethane and the extract analyzed by HPLC with detection by light absorption at 225 nm. Comparison with standards containing known amounts of triazolam revealed that 0.17 mg of > 99% pure triazolam had been collected in the flask, resulting in an aerosol drug mass density of 0.17 mg/L. The aluminum foil upon which the triazolam had previously been coated was weighed following the experiment. Of the 0.6 mg originally coated on the aluminum, all of the material was found to have aerosolized in the 6 s time period, implying a rate of drug aerosol formation of 0.1 mg/s.